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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/917,800	07/31/2001	Donna L. Mendrick	GENE-035/09US	1108

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EXAMINER	
MILLER, MARINA I	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 04/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/917,800	MENDRICK ET AL.	
	Examiner	Art Unit	
	Marina Miller	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *92-129* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *92-129* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' submission filed on 01/05/2006 is acknowledged. Claims 92-129 are pending. Claims 1-91 are cancelled. Claims 92-129 presently are under examination.

Applicants' arguments have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are applied.

Claim Rejections - 35 USC § 112

Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 92-129 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims were previously rejected for lack of enablement for the following reasons:

1) A database comprises data from liver, heart, kidney, testes, and brain, and therefore one cannot predict hepatotoxicity by comparing data from liver to the database;

2) The specification does not disclose whether the comparison in Tables 3A-3S is performed between expression profiles in liver or liver, kidney, testes, kidney, and brain;

3) Not all genes of Table 1 are implicated in liver toxicity;

4) It is not disclosed whether comparison recited in claims 105 and 124 is performed with normal liver tissue or diseased tissue;

Applicants argue that all genes disclosed in Tables 3A-3S are differentially expressed in liver cells and that Tables 3A-3S are specific to liver toxicity. Applicants further argue that the fact that Table 1 discloses genes with unknown pathways and/or genes which are not known to be involved in liver toxicity is irrelevant. Applicants also argue that one of skill in the art would have recognized that liver tissue recited in the instant claims is normal tissue and tissue exposed to an agent. Applicants' arguments have been considered, but are found not responsive.

In response, it is noted that the specification discloses that Tables 3A-3S are generated from a microarray comprising expression data from liver, heart, kidney, testes, and brain (p. 38-39). Therefore, it is reasonable to conclude that genes listed in Tables 3A-3S are expressed in multiple tissues, and one of skill in the art would not know how to predict liver toxicity without undue experimentation. Moreover, to practice the method of predicting liver toxicity, one skilled in the art has to possess or has to know how to make or where to get a database comprising gene expression levels. However, the specification neither discloses nor directs the skilled artisan to where to find and/or how to create the database. The specification only discloses Tables 3A-3S that do not comprise expression levels, but instead comprise parameters such as group mean, group standard deviation, LDA score, *etc*. Also, claim 94 recites comparing gene expression profiles with toxic mean and/or non-toxic mean values. However, the specification does not provide guidance how to compare gene expression levels with mean values.

To further answer the arguments, it is noted that it is not readily apparent that all genes in Tables 3A-3S, which are based on Table 1, are involved to liver toxicity. For example, it is not

clear whether GLGC ID 4097-4168 and 11426 to 11504 are implicated in liver toxicity because their pathways are not known.

Applicants argue that Tables 3I-3J produced from normal liver tissue before the exposure and tissue after the exposure to a toxin. However, it is not readily apparent that the instant clams recite comparison of normal tissue with the tissue exposed to a toxin. For example, Table 3D comprises data directed to necrosis with and without fatty liver wherein the specification does not disclose that the comparison is made for normal and diseased liver tissue.

For the reasons stated above and in the previous office action, the examiner maintains the rejection under 35 U.S.C. 112, first paragraph, for lack of enablement.

Written Description

Claims 92-129 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants amended claims 92 and 111 to recite "genes are selected from the gene sequences listed in ... tables 3A-3S."

It is noted, that the sequence disclosed in Tables 3A-3S are not ALL gene sequences. Some of the sequences actually correspond to mRNA, cDNA, EST, and partial CDS sequences. Therefore, with the exception of SEQ ID's corresponding to gene sequences, the sequences of Tables 3A-3S do meet the written description provision of 35 U.S.C. 112, first paragraph. For example, a sequence identified by NCBI accession ID No. U20796 (GLGC ID NO:90; SEQ ID

NO:1454) is an mRNA partial CDS sequence; a sequence identified by NCBI accession ID No. AA893552 (GLGC ID NO:1562; SEQ ID NO:267) is a mRNA sequence of the 3'end of cDNA of clone RLIAD83; a sequence identified by NCBI accession ID No. AA817829 (GLGC ID NO:1690; SEQ ID NO:46) is an mRNA sequence of the 5'end of cDNA clone 575958, *etc.*, and are not, therefore sequences of "genes." Thus, the instant claims are rejected for lack of written description. The rejection is necessitated by amendment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 92, 106, and 111 are rejected under 35 U.S.C. 102(b) as being anticipated by Farr et al., US Patent 5,811,231.

The claims were previously rejected as anticipated by Farr. Applicants argue that ten genes recited in the instant claims do not correspond to genes disclosed by Farr because Farr does not disclose a single liver toxicity model of any one of Tables 3A-3S wherein each table discloses a single liver toxicity model. Applicants' arguments have been considered, but are found not persuasive.

In the response to the arguments, it is noted that the instant claims do not recite "a single toxicity model." Claims 92 and 111 only recite a random selection of ten genes from the sequences listed in Tables 3A-3S. Farr does disclose ten genes disclosed in the tables (*see* Farr et al., tables 1-2), as set forth in the previous office action. The examiner maintains that Farr

discloses all limitations of claims 92, 106, and 111, and therefore maintains the rejection of claims 92, 106, and 111.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 92, 97-101, 111, and 116-120 are rejected under 35 U.S.C. 103(a) as being unpatentable over Farr et al., US Patent 5,811,231.

The claims were previously rejected as being obvious over Farr et al. Applicants do not specifically address the obviousness rejection over Farr et al. and only argue that Farr does not disclose ten genes from any one of Tables 3A-3S.

In response to the argument, the examiner maintains that Farr et al. discloses ten genes from the tables, as set forth above and in the previous office action, and therefore also maintains the instant rejection.

Claims 92, 97-101, 111, and 126 are rejected under 35 U.S.C. 103(a) as being unpatentable over Farr et al., US Patent 5,811,231, and in view of Lashkari et al., *PNAS*, 94:13057-13062 (1997).

The claims were previously rejected as being obvious over Farr et al. and Lashkari. Applicants do not specifically address the obviousness rejection over Farr et al. and only argue

that Farr does not disclose ten genes from any one of Tables 3A-3S and Lashkari neither provides what Farr lacks nor discloses a method related to the instant method.

In response to the argument, the examiner maintains that Farr et al. discloses ten genes from Tables 3A-3S and all limitations of claims 92 and 111, as set forth above and in the previous office action. Lashkari discloses the limitations of microarray recited in claims 107 and 126. Motivation to combine the references was provide in the previous office action. Therefore, the examiner maintains the rejection of claims 92, 97-101, 111, and 126 under 35 U.S.C. 103(a).

Conclusion

No claims area allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-5, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph. D. can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marina Miller
Examiner
Art Unit 1631

MM

MARJORIE A. MORAN
PRIMARY EXAMINER

Marjorie A. Moran
4/6/06